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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/614,795	07/09/2003	Andrew J. Dannenberg	CRF D-2756 NB	8535

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BACON & THOMAS, PLLC
625 SLATERS LANE
FOURTH FLOOR
ALEXANDRIA, VA 22314

EXAMINER	
ROBERTS, LEZAH	

ART UNIT	PAPER NUMBER
1614	

DATE MAILED: 02/14/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/614,795	DANNENBERG ET AL.	
	Examiner	Art Unit	
	Lezah W. Roberts	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 Nov 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 2* is/are pending in the application.

4a) Of the above claim(s) *3-5* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-2* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This action is being made non-final through no fault of the Applicant.

Response to Amendment

The Applicant's response filed on November 3, 2005 has been received.

Claims 3-5 have been cancelled.

Claims 1-2 have been previously presented.

Claims 1-2 are pending.

Claim Rejections

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

35 U.S.C. 112 Rejections

1) Claim 1 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim recites a method for screening a selective inhibitor of COX-2 for functionality in addition to COX-2 protein inhibition yet the word "functionality" is not clearly defined within the specification. The applicant does not disclose what functionality encompasses or examples of such functions. It is

assumed by the wording of the claim; the word "functionality" refers to how the selective COX-2 inhibitor affects a "COX protein inhibition independent therapeutic activity". The phrase "COX protein inhibition independent therapeutic activity" is defined as "therapeutic activity unrelated to the inhibition of prostaglandin synthesis" (page 3, lines 7-9). The applicant describes select COX protein inhibition independent therapeutic activities as recited in claim 2 but does not adequately disclose a representation of all the possible "COX protein inhibition independent therapeutic activities" that can possibly be screened (a potentially almost infinite set of possibilities).

In regards to the Remarks for the rejection of claim 1 rejected under 35 U.S.C 112, for failing to comply with the written description, Applicant's arguments have been taken into consideration but are not persuasive. Applicant states the term functionality is used with its normal dictionary meaning "of or able to perform a function". The applicant fails to clarify what they think encompasses a function. Therapeutic function may range from downregulation of tyrosine kinase as stated by applicant to a decrease in strokes in patients receiving a COX-2 inhibitor. These two functions represent how broad the term function is. If a COX-2 inhibitor decreases the occurrence or reoccurrence of strokes, that is a function of the COX-2 inhibitor. Therefore the Applicant does not define the metes and bounds to which this term encompasses. The claim is an independent claim and stands on its own merits. In order to make it clear what functionality is being screened, the claim must state it in the body of the claim. The term functionality remains broad and the positive steps only give a small representation of what the functionality is.

2) Claim 2a recites a method of screening which comprises screening for activation of PPRE-luciferase by at least 100 %, which is a result but is not a therapeutic function. The claim indicates the method is to screen for a "COX-2 protein inhibition independent therapeutic function". The claim does not clearly convey what function or therapeutic activity is being measured by monitoring PPRE-luciferase activity. The claim reads as if the activation of PPRE-luciferase is the therapeutic activity, which is not supported by the specification. Although the applicant discloses "the ability of a test compound to stimulate PPRE-luciferase signifies that the test compound activates PPAR-mediated gene transcription", this does not support the claim as written. It also does disclose measuring PPAR activity by luciferase assay but no other assays. It is concluded that activation refers to PPRE-luciferase and not PPAR-mediated gene transcription activation. The applicant also discloses activation by 100% but does not disclose if this refers to a 100% decrease or increase in luciferase activity. It is concluded any change in luciferase activity by 100 % is considered activation of luciferase activity.

In regards to the rejection of claim 2 under 35 U.S.C. 112, first paragraph on the basis that COX-2 protein functionality is unclear, Applicant's response has been taken into consideration but is not persuasive. The Applicant argues luciferase activity indicates PPAR activation. The claim indicates luciferase activity is the independent function, which is not the case. PPAR activation is the therapeutic function and that should be made clear, i.e., downregulation of tyrosine kinase, which is the "therapeutic

function", not how you measure it. Therefore, it must be clearly stated in the claim that this is the activity being screened for, which it does not.

Rejections U.S.C. 102 (b)

The response filed on November 3, 2005 under 37 CFR 1.131 has been considered and is effective to overcome the Vadlamudi reference. Rejection withdrawn.

Rejection U.S.C. 103(a)

Winde et al. discloses a COX-2 inhibitor, sulindac decreased HER-2 expression in rectal mucosa familial adenomatous polyposis patients (FAP) (see abstract).

In regards to the remarks responding to the 103 rejection for Winde et al. in view of Subbaramaiah et. al., Applicant's arguments are partially persuasive. Applicant argues sulindac is not a COX-2 inhibitor. Note that Ferrandina et al. teaches sulindac is a COX-2 inhibitor, thus where Winde teaches sulindac it is a COX-2 inhibitor. Further in view of Lemoult, sulindac is a selective COX-2 inhibitor. It is an inherent property of the sulindac to be a selective COX-2 inhibitor regardless of when the information was disclosed. The time when testing was done is irrelevant since no time limitation was included within the claim.

In regards to the Subbaramaiah et. al. reference, ciglitazone was in the reference, it was also used in the disclosure as one of the compounds tested. It was not clear in the disclosure if it was considered a COX-2 selective inhibitor or not, therefore it was regarded as such. The rejection is withdrawn.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claim 2 is rejected under 35 U.S.C. 101 because the claimed invention lacks patentable utility. The claim recites screening methods for COX-2 selective inhibitors but gives no basis for how or why to use the invention in the specification or why one would want to screen for activation of luciferase by 100%. Specifically, claim 2(a) states the therapeutic function is activation of PPRE luciferase by at least 100%, which means activation of PPAR. Which means it activates transcription but tells you nothing else about how the inhibitor inhibits synthesis or treats a disease. The Applicant fails to disclose specifically why one would want to screen an inhibitor using this method or how this relates to the disclosed diseases or the "real world" context of use such as for use *in vivo*. It is not disclosed how one could screen for a disease using luciferase or how one would determine the mechanism of inhibition. Luciferase is an indicator of activity and is not used *in vivo*. There is no specific or substantial utility for activation of PPAR because it does not tell the mechanism of action without a test of another function that happens during protein synthesis, such as production of the COX-2 protein, product or intermediate. It is unclear how PPAR activation is beneficial for screening a selective COX-2 inhibitor or why it is beneficial to use inhibitors that activate PPAR. Applicant has not disclosed any specific or substantial utility for claimed invention.

Claim Rejections - 35 USC § 102 - Anticipation

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Winde et al. (Cancer Letters 1998).

Winde et al. discloses a COX-2 inhibitor, sulindac (which is a selective COX-2 inhibitor as stated above) decreased HER-2 expression in rectal mucosa familial adenomatous polyposis patients (FAP) (see abstract). The HER-2 protein is overexpressed in breast, gastric, and colon cancer (page 201, column 2). A chemopreventive study was conducted to elucidate the possible influence of sulindac on an oncogenic tyrosine kinase receptor (HER-2) by comparing the HER-2 expression in rectal mucosa of FAP patients undergoing treatment with sulindac with those of several control groups. The control groups included a group of FAP patients that were not treated with sulindac, healthy patients, patients with Crohn's disease and a group of patients with rectal cancer. The FAP control group had a mean HER-2 level of 1639 fm/ml with a confidence interval (CI) of 1155-2122 fm/ml. The sulindac treated group had a mean HER-2 level of 503 fm/ml and a CI of 293-713 after 3 months of low-dose sulindac treatment (page 203, column 2). The reference anticipates the claims insofar as it discloses a selective COX-2 inhibitor having a COX protein independent therapy.

Claims 1-2 are rejected.

No claims allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lezah W. Roberts whose telephone number is 571-272-1071. The examiner can normally be reached on 8:30 - 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Lezah Roberts
Patent Examiner
Art Unit 1614

CHRISTOPHER S. F. LOW
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600